The specification has been amended to correct typographical and spelling errors on pages 7 and 17. Applicants respectfully request that these amendments be entered as they do not introduce new matter.

Claim 28 has been amended by adding that the composition blocks binding of at least one of wild-type enterohemorrhagic *E. coli* (EHEC) and wild-type enteropathogenic *E. coli* (EPEC) bacteria to a mammalian cell. Specific support for this amendment occurs, for example, on page 7, lines 2-7, and page 8, lines 9-13 of the specification as filed. The binding function, as well as methods for measuring binding, are both discussed on pages 17-18. The antibodies of the claimed invention are able to block such binding. Such blockage includes complete blockage or partial blockage, both of which can be readily assessed by the skilled person using the disclosed methods. Thus, the amendment is supported by the specification.

New claim 51 corresponds to claim 28 as filed and also recites cross-reactivity of the antibodies with both EPEC and EHEC. Cross reactivity results when the portion of intimin that elicits antibody formation is homologous between the organisms, and the specification provides that the N-terminal three-quarters of the EPEC and EHEC proteins share 94% identity and would therefore be cross-reactive. New dependent claims 52-55 (which depend from new claim 51) are identical to claims 29-32 as originally filed, and as such introduce no new matter.

**Election/Restriction**

The claims elected in Paper No. 7 are being prosecuted. Applicants do point out that the amendment was made with traverse, albeit without argument.

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## Claim Objections

The Examiner's objection to claim 29 for reciting an abbreviation not defined in the claims has been obviated by the inclusion of the phrase "enterohemorrhagic *E. coli* (EHEC)" in claim 28 as amended. This term is defined as such in the specification (see page 1, lines 14-15) and therefore this amendment introduces no new matter.

## Claim Rejections

Under the numbered paragraphs noted below, the Examiner rejected the claims in light of the recited art. Applicants describe and respond to each rejection as follows.

8. Louie et al.
Rejection under 35 U.S.C. § 102(b)

The Examiner rejected claims 28-29 and 31 as allegedly anticipated by Louie et al. Louie et al. use a GST-intimin$_{O157}$ fusion protein to prepare polyclonal antisera from rabbits and remove nonspecific *E. coli* proteins by adsorption with lysates of uninduced *E. coli*. However, this procedure did not provide anti-intimin antibodies "free of other antibodies specific for an intimin-expressing host bacteria" as required by the instant invention (see amended claim 28 and new claim 51). On page 4088, Louie et al. observe that, "[b]oth anti-GST and anti-GST-intimin$_{O157}$ sera reacted nonspecifically with major outer membrane porins of all strains tested, despite extensive adsorption," indicating the presence of other antibodies specific for intimin-expressing host bacteria. Additionally, Louie et al. state (on page 4090) "[o]ur data suggest that intimin$_{O157}$ contributes minimally if at all to the total adherence of [serotype O157:H7] to HEp-2 cells,"

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thereby teaching that its antibodies are not involved in blocking the binding of wild-type EHEC and EPEC to mammalian cells as now recited in claim 28 as amended. Thus, Louie et al. cannot anticipate nor render obvious the claimed invention.

9. McKee and O'Brien, Abstract B-5
Rejection under 35 U.S.C. § 102(a)

The Examiner has rejected claims 28 and 31 as allegedly anticipated by the McKee abstract. This brief paragraph by two of the three inventors of the instant invention, Dr. Marian L. McKee and Dr. Alison D. O'Brien, does not teach or suggest antibodies which block binding of bacteria as claimed in instant claim 28, nor does it teach antibodies which cross react with both EHEC and EPEC (see new claim 51). Thus this publication does not teach or suggest all of the limitations of the instant invention as now claimed.

10. McKee, Dissertation Abstract
Rejection under 35 U.S.C. § 102(b)

The Examiner has rejected claims 28 and 31 as allegedly anticipated by the McKee dissertation abstract. In order for a publication to qualify as prior art under § 102(b), it must have been published more than one year prior to the effective filing date of the application at issue. The instant application claims benefit of two U.S. Provisional Patent Applications, Serial No. 60/015,657, filed April 19, 1996, and Serial No. 60/015,936, filed April 22, 1996. However, the McKee dissertation and abstract were not publically available until November, 1995 at the earliest, as demonstrated by a declaration to this effect, signed by Ms. Christina Kelley. Thus, the McKee dissertation and abstract are not available as prior art under 35 U.S.C. § 102(b) and cannot anticipate the claimed invention.

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11. de Azavedo et al.
Rejection under 35 U.S.C. § 102(b)

The Examiner has rejected claims 28-31 as allegedly anticipated by de Azavedo et al., asserting that de Azavedo discloses monoclonal antibodies to enterohemorrhagic *E. coli* which would anticipate the instant invention. Although the de Azavedo Canadian patent application describes antibodies to proteins associated with attaching and effacing in EHEC, it neither teaches nor suggests all of the requirements of the Applicants' invention as now claimed. On page 3, de Azavedo teaches that the product of the *eae* gene (i.e., intimin) is "necessary but not sufficient for the formation of the AE lesion," teaching that intimin is not sufficient for binding to mammalian cells. Since de Azavedo believed that intimin was not sufficient for binding, antibodies to intimin which block the binding of *E. coli* bacteria were never considered. Finally, the inventors on this application are three of the authors of the Louie publication, which opines that $intimin_{O157}$ contributes "minimally if at all to the total adherence" of *E. coli* to cultured cells (discussed above, see ¶ 8), again emphasizing that antibodies to such a protein would not be able to be involved in blocking the binding of wild-type EHEC and EPEC to mammalian cells as now recited in amended claim 28. Thus, the de Azavedo antibodies would not block the binding of *E. coli* bacteria as claimed in claim 28 as amended, nor would they cross react with both EHEC and EPEC (see new claim 51). Therefore, de Azavedo et al. cannot anticipate nor render obvious the claimed invention.

12. Acheson et al.
Rejection under 35 U.S.C. § 102(e)

The Examiner has rejected claims 28-31 as allegedly anticipated by Acheson et al., asserting that Acheson's antibodies to invasin anticipate the instant invention. On the contrary,

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Acheson et al.'s invention is built around the concept of using spores of *B. subtilis*, or of other spore-forming bacteria, as a vaccine vector. Figure 3, cited by the Examiner, merely illustrates that the antibodies produced do bind to cells or spheroplasts, but there is no indication that this binding would block *E. coli* binding as claimed in instant claim 28, nor is there any teaching of cross reactivity with both EHEC and EPEC (see new claim 51). Acheson et al. is focused on binding, and fails to appreciate the advantages of blockage of binding of *E. coli*. Thus, Acheson et al. cannot anticipate the claimed invention.

13. Dougan et al., U.S. Pat. No. 5,747,293
Rejection under 35 U.S.C. § 102(e)

The Examiner has rejected claims 28-32 as allegedly anticipated by Dougan et al. The monoclonal antibodies described by Dougan are intended to be of particular use in the detection of EHEC and EPEC. While these antibodies are described as recognizing a specific protein epitope for detection purposes (see Dougan SEQ ID NO: 1), there is no indication that such antibodies would block the binding of bacteria. In column 2, lines13-17, Dougan states that intimin requires the cooperation of other proteins to induce the effacement and attachment lesion, suggesting that intimin alone would not function in binding and thereby teaches away from the use of intimin to produce useful antibodies. Furthermore, Dougan et al. specifically teaches monoclonal antibodies which recognize only EHEC, and not EPEC (column 2, lines 44-46; column 3, lines 20-26). Dougan et al. thus does not teach or suggest antibodies which block binding of bacteria as claimed in instant claim 28, nor does it teach antibodies which cross react with both EHEC and EPEC (see new claim 51). Thus, Dougan et al. cannot anticipate the claimed invention.

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14. Leong et al. (1990)
Rejection under 35 U.S.C. § 102(b)

The Examiner has rejected claims 28-32 as allegedly anticipated by Leong et al. While Leong describes identification of the integrin binding domain of invasin in a different genus (*Yersinia* spp.), they do not provide antibodies which block binding of at least one of wild-type enterohemorrhagic *E. coli* (EHEC) and wild-type enteropathogenic *E. coli* (EPEC) to a mammalian cell, nor antibodies which have cross-reactivity with both EPEC and EHEC. Thus, Leong et al. cannot anticipate the claimed invention.

## CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request the reconsideration of this application and timely allowance of the pending claims.

Please grant any additional extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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